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# Heat Shock Protein as a Mediator Between the Effects of Corticosteroids on Atrial Fibrillation Recurrence After Catheter Ablation

Koyama et al. (1) conducted an excellent study on the prevention of atrial fibrillation recurrence with corticosteroids after radiofrequency catheter ablation. However, the mechanism by which a short course of corticosteroids for 3 days right after catheter ablation could prevent long-term recurrence of atrial fibrillation remains unclear and puzzling. Inflammation and atrial remodeling during the early phase seem to play a role.

In reference to that, I would like to point out that corticosteroids could decrease atrial fibrillation recurrence by stimulating the release of heat shock proteins (HSPs). Corticosteroids induce a heat stress response with the release of HSPs (2). In an in vitro model, artificially up-regulating HSP27 protects against atrial remodeling, which was measured as calcium transient and cell shortening (3). In a canine model, HSP induction attenuates tachypacing-induced decreases in the effective refractory period (ERP) (3). This study also demonstrated that remodeling changes occur in as little as 4 h of tachypacing (3). In another study, overexpressing HSP27 significantly reduced tachypacing-induced myolysis (4).

So far, studies have shown that HSPs have cardioprotective effects at an in vitro level in an animal model. Altering HSP expression at a clinical level has not yet been studied, and it is unclear whether it has any disease modification properties in patients with atrial fibrillation. Future studies should focus on the interactions between corticosteroids, HSPs, and the recurrence of atrial fibrillation after cardioversion and catheter ablation. HSPs could be a novel target for intervention in atrial fibrillation.

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## Reply

We thank Dr. Ng for his constructive suggestions. Unfortunately, we did not examine heat shock proteins (HSPs) in our study (1). However, it is one of the important possible mechanisms that HSPs induced by corticosteroids could prevent atrial electrical remodeling through cardioprotective actions.

It is known that inflammatory responses are closely associated with the occurrence or maintenance of atrial fibrillation (AF). AF occurrences are frequently observed after cardiac surgery. A previous study suggested that inflammatory cytokines such as interleukin-6 (IL-6) are involved in AF occurrences related to cardiac surgery (2). Halonen et al. (3) provided strong evidence that short-duration and low-dose corticosteroid could suppress AF onset after surgery. We believe that the anti-inflammatory action of corticosteroids is an effective therapeutic approach to AF. It is commonly accepted that radiofrequency catheter ablation is an effective therapeutic option for drug-refractory AF. As mentioned in our study, catheter ablation procedures for AF cause relatively large amounts of damage to the atrial tissue due to radiofrequency energy (1). As a result, the acute inflammatory response could be evoked after catheter ablation procedures. Very recently, it was reported that interleukin-6-positive mononuclear cells are recruited to atrial tissue and involved in the arrhythmogenic substrate in the human atrium (4). We hypothesized that these responses could occur in damaged cardiac tissue caused by catheter ablation. This damage could cause infiltration of inflammatory cells such as mononuclear cells. Additionally, these inflammatory responses could cause the electrical and structural remodeling via pro-inflammatory cytokines after catheter ablation, resulting in the AF recurrence. One possible mechanism is that corticosteroids suppress macrophage migration and its release of pro-inflammatory cytokine, thus preventing AF recurrence after catheter ablation.

Mandal et al. (5) provided an interesting study showing that anti-HSP 65 was an important contributor to the risk of postoperative AF. St Rammoss et al. (6) reported that atrial HSP levels negatively correlate with AF incidence after cardiac surgery. These results suggest that HSPs are an important suppressor of AF after